

Remarks

Status of the Claims

By the foregoing amendment, claim 112 is sought to be amended to provide the proper dependency for this claim. Therefore, this amendment does not add new matter, and its entry and consideration are respectfully requested. Upon entry of the foregoing amendment, claims 35-36, 38-66, 69-75, 77 and 79-112 are pending in the application, with claims 35, 39, 52, 69 and 72 being the independent claims.

Summary of the Office Action

In the Office Action dated September 22, 2004, the Examiner has made three rejections of the claims. Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

The Rejection Under 35 U.S.C. § 112, First Paragraph

In the Office Action at pages 2-6, the Examiner has rejected claims 52-68 and 87-91 and 101-106 under 35 U.S.C. § 112, first paragraph, alleging that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse this rejection.

The Examiner contends that the present specification does not provide sufficient basis for the ordinarily skilled artisan to envision embodiments of the claimed invention wherein the nucleic acid encoding a functional antibiotic resistance gene comprises a first portion and a second portion separated by any recombination site sequence. The Examiner

further contends that in view of the present specification, the skilled artisan would not have been able to envision a sufficient number of specific embodiments to describe the broadly claimed genus of nucleic acids. The Examiner states that an applicant claiming a biotechnical invention cannot necessarily claim a genus after only describing a limited number of species. Applicants respectfully disagree with these contentions.

Applicants' remarks made in their previous reply, filed June 24, 2004, are hereby incorporated by reference herein in their entirety. Applicants also offer the following additional remarks to overcome the present rejections. The Examiner's attention is directed to the present specification at page 14, lines 1-15, where several non-limiting examples of recombination sites and recognition sequences are discussed. The Examiner's attention is also directed to page 22, line 15, through page 30, where numerous recombination systems are disclosed, including recombination proteins, recombination sites, and various mutated recombination sites which may be utilized in the practice of the presently claimed invention.

Applicants respectfully submit that the ordinarily skilled artisan would readily recognize that any of these recombination sites and systems can be successfully utilized in the practice of the presently claimed invention.

Applicants respectfully submit that the numerous examples in the present specification which utilize various recombination sites and systems provide the ordinarily skilled artisan with a sufficient basis to envision the full breadth of the present claims. The Examiner's attention is directed to page 19, lines 9-24 describing Figure 2; to Example 2 at page 36 describing Figures 4A-4C; and to Example 5, all of which provide non-limiting examples of nucleic acid molecules within the scope of the present invention comprising various *att* and *lox* sites. The ordinarily skilled artisan would readily recognize that any of

the various recombination sites, including mutated recombination sites, disclosed throughout the present specification may be exchanged for one another in the practice of the presently claimed invention. Applicants submit that the present specification provides disclosure of numerous recombination sites disclosed throughout the present specification, and others that are well-known in the relevant art, that can be used in the practice of the present invention.

The Examiner asserts that "Applicants do not set forth how disclosure of a single embodiment (i.e. loxP) would sufficiently describe a sufficient number of embodiments." Office Action at page 5, lines 13-15. Applicants respectfully submit, as described in detail above and in Applicants' previous reply, the present specification provides disclosure of a great number of recombination sites that may be used in the practice of the present invention. Applicants respectfully submit that the ordinarily skilled artisan would readily recognize that any of these exemplary recombination sites can be used in the practice of the present invention, and hence, the ordinarily skilled artisan would easily be able to recognize a sufficient number of embodiments encompassed by the present invention.

The Examiner is reminded that:

[w]hat constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed.

M.P.E.P. § 2163 at p. 2100-169, first column, lines 25-32. Applicants respectfully submit that the level of skill and knowledge in the art of recombinational cloning is high. The ordinarily skilled artisan in this field would readily recognize that Applicants were in possession of the necessary common attributes or features of the elements possessed by the

members of the genus, as Applicants have described a large number of exemplary recombination sites and antibiotic resistance genes that can be used in the practice of the present invention.

Applicants also wish to remind the Examiner that an applicant is not required to disclose or provide a working example of every species of a given genus in order to meet the written description requirement of 35 U.S.C. § 112 (*see Ex parte Parks*, 30 USPQ2d 1234, 1236 (Bd. Pat. App. Int. 1994) and *In re Alton*, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996)), and subject matter that “might fairly be deduced from the original application” is considered to be described in the application as filed. *Acme Highway Products Corp. v. D.S. Brown Co.*, 431 F.2d 1074, 1080 (6th Cir. 1970) (citations omitted), *cert. denied*, 401 U.S. 956 (1971), *followed by Westphal v. Fawzi*, 666 F.2d 575, 577 (C.C.P.A. 1981). Moreover:

[a] description of a genus of [nucleic acid molecules] may be achieved by means of a recitation of a representative number of [nucleic acid molecules], defined by nucleotide sequence, falling within the scope of the genus

Regents of Univ. of Calif. v. Eli Lilly & Co., 119 F.3d 1559, 1569 (Fed. Cir. 1997).

As noted above, the present specification describes a number of representative examples of the claimed genus of recombination sites, and provides detailed specifications for the physical and/or structural characteristics of other nucleic acid molecules that would fall within the scope of claims 52-68 and 87-91. In so doing, the "representative number" standard under *Eli Lilly*, upon which the Written Description Guidelines (M.P.E.P. § 2163) are based, is clearly met by the present specification. Hence, Applicants respectfully assert that the present specification provides sufficient written description to convey to one of

ordinary skill that Applicants had possession of the full scope of the claimed invention upon filing of the application.

In view of the foregoing remarks, Applicants respectfully request that the rejection of claims 52-68 and 87-91 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

The Rejections Under 35 U.S.C. § 112, Second Paragraph

In the Office Action at pages 6-7, the Examiner has first rejected claims 39-66, 79-96 and 101-106 under 35 U.S.C. § 112, second paragraph, alleging that that terms "recombination site" and "cloning site" are vague and indefinite. Applicants respectfully traverse this rejection.

Applicants respectfully submit that the ordinarily skilled artisan, upon reading the present specification, would readily understand that the term "recombination site" refers to a site-specific recombination site. As noted in Applicants' previous reply, the term "recombination site" was well known in the art at the time of the filing of the present application to mean a site-specific recombination site. The term "recombination site" is used in this context and with this meaning consistently throughout the present specification (*see, e.g.*, p. 26, line 16, though page 30). Hence, one of ordinary skill in the art would readily understand the meaning of the term "recombination site" as it is used in the present claims.

The Examiner also asserts that the dependent claims drawn to nucleic acids comprising specific site-specific recombination sequences (e.g., *loxP*) are vague and indefinite, because such nucleic acids may contain sequences at the recombination site in addition to the site-specific sequence. Applicants respectfully disagree with this assertion.

As discussed in the previous reply, Applicants again submit that the ordinarily skilled artisan would readily understand that indeed, the nucleic acid molecules of the present invention can comprise, and often will comprise, nucleotide sequences at the recombination site in addition to the site-specific recombination sequences. However, this fact alone does not render the recitation of "recombination site" vague or indefinite, as the ordinarily skilled artisan would readily understand the meaning of this term as it is used in the present specification and claims, regardless of whether or not additional nucleotide sequences are also located at or near the recombination site on a given nucleic acid molecule.

In view of the foregoing remarks, Applicants respectfully request that the rejection of claims 39-66, 79-96 and 101-106 under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

The Examiner has also rejected claims 47 and 62 under 35 U.S.C. § 112, second paragraph, alleging that the term "one cloning site" is vague and indefinite, as it is unclear what the term encompasses. Applicants respectfully disagree with this allegation.

As discussed in the previous reply, Applicants respectfully submit that the ordinarily skilled artisan would readily understand that the term "one cloning site" encompasses any site within a given nucleic acid molecule which allows for insertion of a desired nucleic acid sequence. The Examiner's attention is drawn to the present specification at page 32, line 27, through page 33, line 2, where the vector pEZR602 shown in Figure 3D is described. The vector pEZR602 comprises "*loxP* and *loxP511* sites flanking a multiple cloning site." Referring then to Figure 3D, the positions of the *loxP* and *loxP511* sites and the multiple cloning site region between the two sites are clearly shown.

As the Examiner has stated, "[Multiple Cloning Site] MPS would readily be understood by one of ordinary skill in the art." Office Action at page 7, lines 20-21. Applicants respectfully submit that the ordinarily skilled artisan in the fields of molecular biology and/or recombinational cloning would readily understand that "one cloning site" is a single cloning site, and that multiple such single cloning sites make up a "multiple cloning site." Hence, Applicants respectfully submit that the ordinarily skilled artisan would readily understand what is meant by the term "one cloning site" and hence, this term is neither vague nor indefinite. In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 47 and 62 under 35 U.S.C. § 112, second paragraph.

The Rejections Under 35 U.S.C. § 112, First Paragraph

In the Office Action at page 8, the Examiner has rejected claims 35-36, 38-66, 69-75 and 79-112 under 35 U.S.C. § 112, first paragraph, alleging that the phrase "immediately adjacent" does not have literal support in the specification. Applicants respectfully traverse this rejection.

Applicants respectfully submit that the phrase "immediately adjacent" would be readily understood by the ordinarily skilled artisan to mean that the recombination sites and the related genes, portions of genes, etc., have no intervening nucleotides between them. To demonstrate exemplary support for this phrase, the Examiner's attention is directed to the present specification at Figure 4C and Figures 8B, 8I and 8J. Figure 4C depicts the pECZ 1003 vector, showing the SP6 promoter located "immediately adjacent" to a *loxP* site (bottom right hand corner of vector pEYC 1003). In Figures 8B, 8I and 8J, each of the

vectors depicted in these figures contains a recombination site (e.g., *attR1*) located "immediately adjacent" to a GST gene. The ordinarily skilled artisan would readily understand that the orientation depicted in these figures represents a recombination site "immediately adjacent" to a related gene or promoter. Applicants therefore respectfully submit that there is sufficient literal support for the phrase "immediately adjacent" in the present application such that the ordinarily skilled artisan would readily understand this phrase as it is used in the present claims.

Conclusion

All of the stated grounds of rejection have been properly traversed or otherwise overcome. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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